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# Evidence from prospective cohort studies did not support the introduction of dietary fat guidelines in 1977 and 1983: A systematic review

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**What are the new findings?**

* Dietary recommendations were introduced in the US (1977) and in the UK (1983) to i) reduce overall fat consumption to 30% of total energy intake and ii) reduce saturated fat consumption to 10% of total energy intake. RCT evidence available at the time did not support the introduction of these dietary fat guidelines. This study finds that epidemiological evidence at the time did not support the introduced dietary fat guidelines.
* No prospective cohort study available to dietary guideline committees found any association between total fat intake and deaths from heart disease.
* No prospective cohort study available to dietary guideline committees found any association between saturated fat intake and deaths from heart disease in the same population.
* All RCT and epidemiological evidence available for the consideration of the dietary guideline committees had been undertaken on men alone. Evidence available at the time could not be generalised to women.

**How might this impact on clinical practice?**

***** Public health advice on dietary fat has prevailed since 1977/1983 in the absence of supporting evidence. The US 2015 dietary guidelines excluded recommendations for total fat for the first time, but maintained the advice to restrict saturated fat. The pool of evidence does not support this recommendation. The UK advice has not changed since 1983. Dietary advice in the UK and the US at least, need re-examination.

* Protein is present in all foods, except pure fats and sucrose, and thus tends to form approximately 15% of total calorie intake. Restricting total fat intake to 30% concomitantly sets a carbohydrate intake of 55%. Diabetes and obesity have increased since guidelines to restrict fat intake. This association needs examination.

## Abstract (250 words)

**Objectives**: National dietary guidelines were introduced in 1977 and 1983, by the United States (US) and United Kingdom (UK) governments to reduce coronary heart disease (CHD) mortality by reducing dietary fat intake. Our 2015 systematic review examined RCT evidence available to the dietary committees at the time; we found no support for the recommendations to restrict dietary fat. What epidemiological evidence was available to the dietary guideline committees in 1983?

**Methods**: A systematic review of prospective cohort studies, published prior to 1983, which examined the relationship between dietary fat, serum cholesterol and the development of CHD.

**Results**: Across 6 studies, involving 31,445 participants, there were 1,521 deaths from all-causes and 360 deaths from CHD during the mean follow-up of 7.5 ± 6.2 years. The death rates were 4.8% and 1.1% from all-causes and CHD respectively.

One study included men with previous heart disease. The death rate from CHD for those with, and without previous myocardial infarction was 20.9%. and 1.0% respectively. None of the six studies found a significant relationship between CHD deaths and total dietary fat intake. One of the six studies found a correlation between CHD deaths and saturated dietary fat intake across countries; none found a relationship between CHD deaths and saturated dietary fat in the same population.

**Conclusions**: 1983 dietary recommendations for 220 million US and 56 million UK citizens lacked supporting evidence from RCTs or prospective cohort studies. The extant research had been undertaken exclusively on males, so lacked generalisability for population-wide guidelines.

## Introduction

US public health dietary advice was announced by the Select Committee on Nutrition and Human needs in 1977[1] and was followed by UK public health dietary advice issued by the National Advisory Committee on Nutritional Education in 1983.[2] Dietary recommendations in both cases focused on reducing dietary fat intake; specifically to i) reduce overall fat consumption to 30% of total energy intake and ii) reduce saturated fat consumption to 10% of total energy intake.

The recommendations were intended to address mortality from coronary heart disease (CHD). In 2015, we published a systematic review and meta-analysis,[3] which reported that evidence from randomised controlled trials (RCTs), available to the dietary guideline committees, did not support the introduced dietary fat recommendations. This systematic review extends this work by re-examining the totality of epidemiological evidence available at the time the dietary fat guidelines were introduced.

The most comprehensive population study undertaken was the Seven Countries Study.[4] This reported that CHD "tended to be related" to serum cholesterol values and that these in turn "tended to be related" to the proportion of calories provided by saturated fats in the diet.[5] Keys acknowledged that epidemiological studies could reveal relationships, not causation.[4] RCTs provide the best evidence.[6]

While the UK nutritional guidelines[2] made reference to the Seven Countries Study, the US committee document[1] did not. Neither publication made reference to any of the RCTs available at that time. However, the US Committee report reported data from the non-randomised, cross-over trial, the Finnish Mental Hospital Study.[7 8]

Although a number of reviews of prospective cohort studies have been undertaken,[9-11] no review has examined the epidemiological evidence available at the time dietary fat guidelines were introduced. These dietary fat guidelines have prevailed until 2016 and thus the validity of their evidence base remains important to examine. UK dietary fat guidelines are unchanged. The Dietary Guidelines for Americans, issued in January 2016,[12] were conspicuously silent on the subject of total fat, but reiterated that saturated fat should be restricted to no more than 10% of calorie intake.

This systematic review will assess if the published prospective cohort studies available to the dietary committees supported their recommendations on dietary fat. With this in mind, we hypothesised that prospective cohort study evidence available to the dietary committees at the time of issuing recommendations did not support the contention that reducing dietary fat intake would contribute to a reduction in CHD risk or related mortality.

## Methods

This systematic review uses the Meta-analysis Of Observational Studies in Epidemiology methodology (MOOSE).[13] MOOSE uses parts of the Cochrane methodology for systematic review and meta-analysis of RCTs, Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA), for example the figure for presenting search methodology.[14]

Cross-sectional studies cannot determine cause and effect. For this reason, and to adhere to best practice evidence available, this review has focused on prospective cohort studies.[15]

### *Search strategy*

A search was undertaken to identify prospective cohort studies that examined the relationship between dietary fat intake, serum cholesterol and mortality from CHD. Exclusion criteria were: clinical trials; cross-sectional studies; case control studies. Inclusion criteria were: prospective cohort studies; participants were human adults; primary study outcome was CHD mortality; data related to dietary fat consumption were available; data on CHD mortality and serum cholesterol measurements were available.

The period searched was up to 5th September 1983, as this was the date of the UK dietary guideline committee publication.[2] In practical terms, the UK publication would have been in preparation, review and print for some weeks or months before this date. However, the search found that no relevant observational studies were published in 1983, giving confidence that available studies could have been considered. The US dietary guidelines were first issued in February 1977 and so publications before and after this date were separated to clarify which evidence was available to each committee.[1]

Searches of the literature were performed using MEDLINE, Embase and the Cochrane Library. AMED and SIGLE (grey literature sources) were not relied upon, as their periods covered were not compatible: from 1985 and 1992 respectively (Fig. 1).[16 17]

*Selection of studies*

Of 285 identified articles, 253 were rejected upon review of the title and abstract. Of these, 52 were rejected for being review articles. 54 were commentaries, editorials or letters. 29 were clinical trials, 11 were not observational studies. 28 related to conditions other than heart disease, primarily cancer, diabetes, hypertension and pregnancy. There were 14 studies where animals or children/adolescents were the primary focus. 26 were articles about pharmacology/blood analysis. 22 were rejected for being related to a particular food or supplement, rather than dietary fat. A further 12 papers were educational material and 5 reviewed dietary compliance in nutritional studies. 32 papers remained. 18 were rejected on closer inspection of the full paper: 9 were reviews, commentaries or expert opinion pieces; 4 were cross sectional/cluster observation studies; 3 were papers on the same study which had no endpoint data; 1 was educational material and the final 1 was a study of blood clotting. 14 met the inclusion criteria. No case control studies or retrospective cohort studies were found, so no data were lost with the inclusion criteria of prospective cohort studies. Where an abstract was unavailable, the publication type, journal name and meta-tags were reviewed to assess if the article should be rejected (for example "letter", "clinical trial", "paediatric"). Copies of the remaining articles were obtained from university libraries or the British Library.

Once duplication was removed, the remaining 14 papers produced 4 articles documenting 6 studies.[4 18-20] The four articles were hand searched for references to the earliest available publications. The six studies were: The Western Electric Study;[18 21] The Puerto Rico Heart Health Program;[19 22 23] The Seven Countries Study;[4] The Framingham Heart Study;[19 24] The Honolulu Heart Program;[19 25 26] and a study conducted in London and the South East[20].

To ascertain the validity of eligible observational studies, a pair of reviewers (ZH and BD) worked independently to determine which studies met the inclusion criteria. The same six were agreed upon. Risk of bias was further assessed using the Cochrane Collaboration assessment tool for component parts relevant to observational studies, defined as follows: selection bias (cohort appropriately reflected wider population characteristics); detection bias (blinding of outcome assessment); attrition bias (incomplete data outcome); and reporting bias (selective reporting) (Fig. 2).[27]

*Data Extraction*

Table 1 details data extraction of: study name; participant characteristics; whether free from CHD at study entry; years of follow-up; outcomes related to serum cholesterol, total dietary fat and saturated dietary fat for those who developed/died from CHD and those who didn't. Other significant associations with CHD, reported by the studies, have been extracted.

The process of data extraction revealed some gaps. The Western Electric Study was the only study with complete data for serum cholesterol, total fat and saturated fat in the form in which the development of CHD could be contrasted with those who remained CHD-free.[21] These data were not available for CHD mortality. The Seven Countries Study reported correlation coefficients for the relationship between serum cholesterol, total fat, saturated fat and CHD for different

countries.[4] It did not report dietary fat intake for participants who developed CHD vs. those who didn't and it did not report dietary fat intake in comparable measurements, e.g. grams, or proportion of calorie intake. The London Bus and Bank Study did not report saturated fat data and reported serum cholesterol and total fat in tertiles, which impaired interpretation.[20] The three studies of Framingham, Honolulu and Puerto Rico did not report serum cholesterol data in relation to CHD.[19 22 24 25] These three studies reported total fat and saturated fat in an optimal way for analysis: the dietary fat intake in grams for those who died from CHD vs. those who didn't.

No one study satisfied all inclusion criteria. The decision was taken to include all six prospective cohort studies available to the dietary committees, with deficiencies noted. This decision was supported by the fact that the UK dietary guidelines publication referenced The Seven Countries Study and the studies of Framingham, Hawaii/Honolulu, London and Puerto Rico.[19 20 26 28]

*Statistical Analysis*

The data available are not conducive to meta-analysis. Three of the studies are presented in a comparable format, but meta-analysis was not possible on these alone, as the information required for dichotomous or continuous analysis was not available.[19 22 24 25] The data presented in the other three studies was in different formats and also lacked the information that would enable meta-analysis to be undertaken.[4 20 21] Table 1 presents the available data in the absence of forest plots being possible. Table 1 illustrates the lack of significant findings.

Table 1 Outcome data from included prospective cohort studies for: study name; participant number and age range; years of follow-up; serum cholesterol, total fat and saturated fat for CHD-free vs. CHD deaths[22 24 25] or CHD-free vs. development of CHD[4 20 21]; and other significant associations found.

| Study | Men/Age | CHD-free? | Follow-up yrs | Deaths All-cause/CHD | Cholesterol CHD/Non | Total fat CHD/Non | Sat fat CHD/Non | Other Significant associations with CHD |
|---|---|---|---|---|---|---|---|---|
| Western Electric Study[21] | 1,989 (40-55) | Y | 4 | 38/13 | CHD/Non 272/247 mean mg/dl | CHD/Non 148/152 g/day (*) | CHD/Non 59/59 g/day (*) | Age of death of father, smoking, coffee, elevated blood pressure |
| Seven Countries Study[4] Note 1 | 12,770 (40-59) | 98% | 5 | 588/158 | r = 0.76 | r = 0.40 (*) | r = 0.84 | Previous MI. NO association found with CHD & activity, smoking or weight |
| The following data were available to the UK Committee only: | | | | | | | | |
| London bank and bus study[20] | 337 (30-67) | Y | 20 | 51/26 | Note 2 3-5.6 7 5.6-6.5 13 6.5-8.6 16 | Note 3 (*) 30-39% 18 38-43% 10 41-56% 17 | N/A | Age of participant. Smoking. Higher calorie intake/cereal fibre & lower CHD |
| Framingham[19 24] | 859 (45-64) | Y | 4 | 47/14 | N/A | CHD death/alive 112/114 g/day (*) | CHD death/alive 46/44 g/day (*) | Higher calorie intake & lower CHD. Higher alcohol intake & lower CHD |
| Honolulu[19 25] | 7,272 (45-64) | Y | 6 | 395/78 | N/A | CHD death/alive 86/87 g/day (*) | CHD death/alive 32/32 g/day (*) | Higher calorie intake & lower CHD. Higher starch intake & lower CHD. Higher alcohol intake & lower CHD |
| Puerto Rico[19 22] | 8,218 (45-64) | Y | 6 | 402/71 | N/A | CHD death/alive 94/96 g/day (*) | CHD death/alive 34/36 g/day (*) | Higher calorie intake & lower CHD. Rural living & lower CHD |
| TOTAL (6 studies) | 31,445 | | | 1,521/360 | | | | |

Table notes: N/A = data not available; MI = Myocardial Infarction

(*) Not statistically significant

Note 1: The Pearson correlation coefficients presented in this row represent 13 cohorts (both Japanese and the Rome railroad cohorts were missing). The coefficients represent the relationship between serum cholesterol, total dietary fat and saturated fat intake for the 13 cohorts and CHD deaths and infarctions. Data for CHD deaths alone were not presented. Data for men without heart disease on entry were not available. The data did not compare fat/cholesterol of those with CHD vs. those without. The correlations apply to fat/cholesterol data for cohorts relative to each other.

Note 2: Tertiles of cholesterol in mmol/l and number of CHD cases, not deaths, in each tertile.

Note 3: % of dietary intake accounted for by total fat and number of CHD cases, not deaths, in each tertile.

## Results

*Participants and Study Design*

The six identified prospective cohort studies included 31,445 male participants. All but 337 participants[20] were over the age of 40 at baseline and were followed for a minimum of 4 years and a maximum of 20 years.

The mean duration of the six cohorts was 7.5 ± 6.2 years. The weighted mean duration (person years by participants) was 5.6 ± 0.8 years.

Five cohort studies excluded men with previous heart disease. The one study that included men with previous heart disease enabled examination of men healthy at baseline in some circumstances.[4]

All studies had complete outcome data, showing no evidence of attrition bias (Fig. 2). Two studies were unclear in the assessment of blinding of outcome.[4 21] The three comparator population studies showed no evidence of selection bias.[19 22 24 25] The London Bus and Bank Study[20] and The Western Electric Study[21] were assessed as having some selection bias for drawing from limited occupations and/or corporations. The selection bias in The Seven Countries Study was stronger, having initially been informed by Keys' analysis of country data[29] and having subsequently relied greatly upon friendship for cohort selection.[28] Five studies were judged low risk for reporting bias, as there was no evidence of any data being withheld. The Seven Countries Study was judged as unclear for reporting bias, as the presentation of data according to thresholds introduced subjectivity (Fig. 2).[27]

In the absence of meta-analysis, statistical review of study heterogeneity was not possible. The studies were homogenous in their focus on men; largely free from previous heart disease and in their study aims to review the impact of dietary fat on CHD mortality for a follow-up period of at least four years. The age of participants was an area of homogeneity: three of the studies included men aged 45-64 (52% of participants);[19 22 24 25] two of the studies included men between 40 and 55 or 59 (47% of participants);[4 21] only one study, accounting for 1% of participants, included a wider age range of 30-67.[20]

Areas of heterogeneity were related to the populations chosen. London bankers, Japanese fishermen, American railroad workers and Puerto Rican farmers, like all the cohorts studied, differed by location, climate, politics, income, ethnicity, genetics, traditional diet, soil quality, and other confounding factors.

*Examination of the dietary guidelines*

None of the six cohorts examined either of the introduced dietary guidelines: a total fat consumption of 30%, or a saturated fat consumption of 10%, of energy intake. Three studies examined the total fat intake and the saturated fat intake, as a percentage of calorie intake, for men who died from CHD compared to men who remained alive.[19 22 24 25] One study examined the total fat intake and the saturated fat intake, as a percentage of calorie intake, for men who developed CHD compared to those who didn't (the comparison was not available for CHD deaths).[21] One study reviewed total dietary fat in tertiles and noted no difference in the saturated fat intake of men in different calorie intake tertiles.[20] One study compared total and saturated fat intake by 7 countries and 16 cohorts, as opposed to by men who developed CHD compared with those who didn't in each region.[4]

*Outcomes: All-cause mortality*

Across 6 studies, involving 31,445 participants, there were 1,521 deaths from all-causes during the period of follow-up. The death rate from all-causes was 4.84%, during the mean follow-up of 7.5 ± 6.2 years.

*CHD mortality*

Across 6 studies, involving 31,445 participants, there were 360 deaths from CHD during the period of follow-up. The death rate from CHD was 1.14%, during the mean follow-up of 7.5 ± 6.2 years.

The death rates contrast with the 30% death rate for the six RCTs available to the dietary guideline committees[3] and reinforce the high death rate in secondary studies. The one study that included men with previous heart disease found that the death rate from CHD for those with pre-existing MI was 20.9%. The death rate from CHD for those without previous MI was 1.0%.[4]

*Significance reported by the studies*

None of the six studies found any significant relationship between CHD deaths and total dietary fat intake. One of the six studies found a statistically significant relationship between CHD deaths and saturated dietary fat intake.[4]

*Serum cholesterol levels*

One of the studies found a statistically significant association between CHD incidence and mean serum cholesterol[21] and another of the studies found a statistically significant association between CHD deaths and infarctions and median serum cholesterol.[4]

**Discussion**

The main findings of this systematic review are that the epidemiological evidence available to the dietary committees did not support the introduction of dietary fat guidelines. There were two prospective cohort studies available to the US committee,[4 21] neither were referenced. An additional four were available to the UK committee,[19 20 22 24 25] one of which was referenced.[4] All available data was not taken into account by the dietary guideline committees and it would not have supported the introduced guidelines had it been considered.

Four of the studies found a significant relationship between higher calorie intake and lower incidence of CHD.[19 20 22 24 25] The Framingham and Honolulu studies found a significant relationship between higher alcohol intake and lower incidence of CHD.[19 24 25] The London and Honolulu studies found a significant relationship between higher starch/cereal intake and lower incidence of CHD.[20 25] Affluence and/or activity levels could have been confounding variables in these findings.

*Design limitations*

As was found with the review of RCT evidence in Harcombe *et al*,[3] the fundamental design limitation of epidemiological evidence available to inform the dietary committees of 1977 and 1983 was that all studies included men only. The epidemiological evidence available at the time of dietary guidelines being introduced had largely evaluated primary prevention men, while the RCTs available at the time had largely studied secondary prevention males.

One study alone provided support for the diet-heart hypothesis.[4] This study suffered the most serious limitations: first of selection bias and second of not comparing the development of CHD against non development of CHD in each cohort. Rather it was an inter country comparison, comparing the development of CHD in one cohort/country with the development of CHD in another cohort/country, which therefore introduced many other confounders.

The summary volume of The Seven Countries Study asserted that smoking, activity levels/exercise and weight played no part in CHD; blood pressure had some observed pattern and CHD tended to be related to total cholesterol and the average proportion of calories provided by saturated fats in the diet.[5]

By 1960, The Framingham Heart Study had found that smoking increased the risk of heart disease.[30] By 1967 the same study had found that exercise had a positive impact on heart disease and weight had an adverse impact.[31] In 1953, Morris *et al* demonstrated the benefit of vigorous physical activity to cardiovascular health.[32] Published in 1970, the conclusions of The Seven Countries Study were contrary to evidence of the time. Importance was assigned to a study for its

cholesterol and saturated fat findings, which contradicted contemporary evidence about smoking, activity and weight.

*Study conclusions*

Five of the studies made no mention of dietary fat in their conclusions. The Western Electric Study concluded: "No relation was encountered between body weight, mean blood sugar levels, lipoprotein lipase levels, or diet (other than coffee), and the development of coronary heart disease" (p30).[21] Morris *et al* identified healthy and unhealthy patterns of behaviour: "Meanwhile, a pattern of healthy living may have been identified: high energy intake and expenditure, high intake of cereal fibre, no cigarettes, with relatively little proneness to heart attack; and another behaviour pattern, of low energy intake and physical inactivity, low intake of cereal fibre, smoking cigarettes-carrying a relatively high risk" (p.1313).[20] The 1981 publication combining the Framingham, Honolulu and Puerto Rico cohorts summarised the findings of the three studies together: "In conclusion, men who developed MI or died of CHD consumed significantly fewer calories (but weighed more) and consumed less alcohol than average" (p.514).[19]

The verbatim findings of The Seven Countries Study were: "The incidence rate of CHD tends to be directly related to the distributions of serum cholesterol values"; "The average serum cholesterol values of the cohorts tended to be directly related to the average proportion of calories provided by saturated fats in the diet"; and "The CHD incidence rates of the cohorts are just as closely related to the dietary saturated fatty acids as to the serum cholesterol level"(p.I-194).[5]

The Seven Countries Study was available to both dietary committees. While the UK nutritional guidelines[2] made reference to The Seven Countries Study, the US committee document[1] did not. However, the US committee document reported that: "The basic research is strongly corroborated by epidemiological studies of populations throughout the world who live quite well on a diet containing as little as 10 percent calories from fat" (p.XL)[1] and the only study of populations throughout the world at that time was The Seven Countries Study.

*Other associations*

Keys reported correlation coefficients as follows: median serum cholesterol and saturated fat as a percentage of calories r = 0.89 (p.I-170); median serum cholesterol and CHD deaths and infarctions (data for CHD deaths alone were not presented) per 100 people r = 0.76 (p.I-172); CHD deaths and infarctions and saturated fat as a percentage of calories: r = 0.84 (p.I-174); and CHD deaths and infarctions and total fat as a percentage of calories r = 0.40 (p.I-173).[33]

These correlation coefficients established strong relationships between the component parts of the diet-heart hypothesis, using saturated, not total, dietary fat and using CHD deaths and infarctions. However, strong correlations were found with CHD and other factors, as different as animal protein and television sets, with Gross Domestic Product and living standards suggested as the confounding and possibly causal variables.[34 35]

The 25 year follow-up to The Seven Countries Study[36] calculated Pearson correlation coefficients for mean serum cholesterol levels at baseline and CHD deaths at 5, 10, 15, 20 and 25 years of follow-up. The Pearson correlation coefficient was calculated as 0.72 for baseline cholesterol and CHD deaths at 25 years. The data in the 1993 Menotti article has been examined to repeat the correlations found with CHD death rates and mean serum cholesterol to understand the data and methodology used. The same methodology was then used to explore alternative correlations. The strongest relationship found was for CHD death rates and the latitude of the country or cohort in The Seven Countries Study.[37] The correlation coefficient for CHD deaths and latitude of the cohort was 0.93. The correlation coefficient for CHD deaths and latitude of the country was 0.96. While Keys did find a strong association with median serum cholesterol and CHD deaths, there were stronger associations that were discoverable.

The latitude finding offers an alternative explanation for the observed relationship with cholesterol and CHD. Vitamin D is made when sunshine synthesises cholesterol in skin membranes.[38] In cohorts further away from the equator, cholesterol is less able to be turned into vitamin D. Population mean serum cholesterol levels are higher and concomitantly population mean vitamin D levels are lower. Higher CHD could be associated with lower vitamin D, with cholesterol a marker, not a maker, of heart disease.[39]

Harcombe *et al*[3] reported that the dietary fat guidelines were not supported by RCT evidence available at the time of their introduction. This systematic review finds that the prospective cohort study evidence available at the time did not support the introduced dietary guidelines. Both reviews reported serious limitations with the availability of primary prevention, both-sex, studies, which are the ones most likely to have generalisability for whole populations.

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**References**


1. Select Committee on Nutrition and Human Needs. *Dietary goals for the United States*. First ed. Washington: U.S. Govt. Print. Off., February 1977.
2. National Advisory Committee on Nutritional Education (NACNE). A discussion paper on proposals for nutritional guidelines for health education in Britain. London: The Health Education Council, 1983.
3. Harcombe Z, Baker JS, Cooper SM, et al. Evidence from randomised controlled trials did not support the introduction of dietary fat guidelines in 1977 and 1983: a systematic review and meta-analysis. Open Heart 2015;**2**(1) doi: 10.1136/openhrt-2014-000196[published Online First: Epub Date]|.
4. Keys A. Coronary heart disease in seven countries I. The study program and objectives. Circulation 1970;**41**(I-1-I-8) doi: 10.1161/01.CIR.41.4S1.I-1[published Online First: Epub Date]|.
5. Keys A. Coronary heart disease in seven countries Summary. Circulation 1970;**41**(I-186-I-195) doi: 10.1161/01.CIR.41.4S1.I-186 [published Online First: Epub Date]|.
6. Barton S. Which clinical studies provide the best evidence? The best RCT still trumps the best observational study. BMJ 2000;**321**(7256):255-6
7. Turpeinen O, Karvonen MJ, Pekkarinen M, Miettinen M, Elosuo R, Paavilainen E. Dietary prevention of coronary heart disease: the Finnish Mental Hospital Study. Int J Epidemiol 1979;**8**(2):99-118
8. Miettinen M, Turpeinen O, Karvonen MJ, Pekkarinen M, Paavilainen E, Elosuo R. Dietary prevention of coronary heart disease in women: the Finnish mental hospital study. Int J Epidemiol 1983;**12**(1):17-25
9. Skeaff CM, Miller J. Dietary fat and coronary heart disease: summary of evidence from prospective cohort and randomised controlled trials. Ann. Nutr. Metab. 2009;**55**(1-3):173-201 doi: 10.1159/000229002[published Online First: Epub Date]|.
10. Siri-Tarino PW, Sun Q, Hu FB, Krauss RM. Meta-analysis of prospective cohort studies evaluating the association of saturated fat with cardiovascular disease. The American journal of clinical nutrition 2010;**91**(3):535-46 doi: 10.3945/ajcn.2009.27725[published Online First: Epub Date]|.
11. Chowdhury R, Warnakula S, Kunutsor S, et al. Association of Dietary, Circulating, and Supplement Fatty Acids With Coronary Risk: A Systematic Review and Meta-analysis. Ann. Intern. Med. 2014;**160**(6):398-406 doi: 10.7326/M13-1788[published Online First: Epub Date]|.
12. U.S. Department of Health and Human Services and U.S. Department of Agriculture. 2015 - 2020 Dietary Guidelines for Americans. 8th Edition.: Available at http://health.gov/dietaryguidelines/2015/guidelines/. 2015.
13. Stroup DF, Berlin JA, Morton SC, et al. Meta-analysis of observational studies in epidemiology: A proposal for reporting. JAMA 2000;**283**(15):2008-12 doi: 10.1001/jama.283.15.2008[published Online First: Epub Date]|.
14. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. J. Clin. Epidemiol. 2009;**62**(10):1006-12 doi: 10.1016/j.jclinepi.2009.06.005[published Online First: Epub Date]|.
15. Song JW, Chung KC. Observational Studies: Cohort and Case-Control Studies. Plast. Reconstr. Surg. 2010;**126**(6):2234-42 doi: 10.1097/PRS.0b013e3181f44abc[published Online First: Epub Date]|.
16. National Institute of Clinical Excellence (NICE). Journals and databases. Secondary Journals and databases 2014. http://www.library.nhs.uk/help/resource.
17. SIGLE System for Information on Grey Literature in Europe. Grey Literature Network Service, Founded 1992.

18. Shekelle RB, Shryock AM, Paul O, et al. Diet, Serum Cholesterol, and Death from Coronary Heart Disease. New England Journal of Medicine 1981;**304**(2):65-70 doi: doi:10.1056/NEJM198101083040201[published Online First: Epub Date]|.
19. Gordon T, Kagan A, Garcia-Palmieri M, et al. Diet and its relation to coronary heart disease and death in three populations. Circulation 1981;**63**(3):500-15 doi: 10.1161/01.cir.63.3.500[published Online First: Epub Date]|.
20. Morris JN, Marr JW, Clayton DG. Diet and heart: a postscript. BMJ 1977;**2**(6098):1307-14 doi: 10.1136/bmj.2.6098.1307[published Online First: Epub Date]|.
21. Paul O, Lepper MH, Phelan WH, et al. A Longitudinal Study of Coronary Heart Disease. Circulation 1963;**28**(1):20-31 doi: 10.1161/01.cir.28.1.20[published Online First: Epub Date]|.
22. Garcia-Palmieri MR, Feliberti M, Costas R, Jr., et al. An epidemiological study on coronary heart disease in Puerto Rico: The Puerto Rico Heart Health Program. Bol. Asoc. Med. P. R. 1969;**61**(6):174-9
23. Garcia-Palmieri MR, Tillotson J, Cordero E, et al. Nutrient intake and serum lipids in urban and rural Puerto Rican men. The American journal of clinical nutrition 1977;**30**(12):2092-100
24. Gordon T, Kannel WB. The Framingham Massachusetts Study twenty years later. In: Kessler I, Levin M, eds. The Community as an Epidemiologic Laboratory; A Casebook of Community Studies. Baltimore: Johns Hopkins Press, 1970:123-46.
25. Kagan A, Harris BR, Winkelstein W, Jr., et al. Epidemiologic studies of coronary heart disease and stroke in Japanese men living in Japan, Hawaii and California: demographic, physical, dietary and biochemical characteristics. J. Chronic Dis. 1974;**27**(7-8):345-64
26. Yano K, Rhoads GG, Kagan A, Tillotson J. Dietary intake and the risk of coronary heart disease in Japanese men living in Hawaii. The American journal of clinical nutrition 1978;**31**(7):1270-9
27. Higgins JPT, Altman DG, Gøtzsche PC, et al. *The Cochrane Collaboration's tool for assessing risk of bias in randomised trials*, 2011.
28. Keys A. *Seven countries: a multivariate analysis of death and coronary heart disease*: Harvard University Press, 1980.
29. Keys A. Atherosclerosis: a problem in newer public health. J. Mt. Sinai Hosp. N. Y. 1953;**20**(2):118-39
30. Dawber TR. Summary of recent literature regarding cigarette smoking and coronary heart disease. Circulation 1960;**22**:164-6
31. Kannel WB. Habitual level of physical activity and risk of coronary heart disease: the Framingham study. Can. Med. Assoc. J. 1967;**96**(12):811-2
32. Morris JN, Crawford MD. Coronary Heart Disease and Physical Activity of Work. BMJ 1958;**2**(5111):1485-96
33. Keys A. Coronary heart disease in seven countries XVII. The Diet Circulation 1970;**41**(I-162-I-183) doi: 10.1161/01.CIR.41.4S1.I-162[published Online First: Epub Date]|.
34. Yerushalmy J, Hilleboe HE. Fat in the diet and mortality from heart disease; a methodologic note. N. Y. State J. Med. 1957;**57**(14):2343-54
35. Yudkin J. Diet and coronary thrombosis: Hypothesis and fact. The Lancet 1957;**270**(6987):155-62
36. Menotti A, Keys A, Kromhout D, et al. Inter-cohort differences in coronary heart disease mortality in the 25-year follow-up of the seven countries study. European journal of epidemiology 1993;**9**(5):527-36
37. Harcombe Z. *The Obesity Epidemic: What caused it? How can we stop it?* York, UK: Columbus Publishing, 2010.
38. Gillie O. Sunlight robbery: a critique of public health policy on vitamin D in the UK. Molecular nutrition & food research 2010;**54**(8):1148-63 doi: 10.1002/mnfr.200900589[published Online First: Epub Date]|.

39. Scragg R. Seasonality of cardiovascular disease mortality and the possible protective effect of ultra-violet radiation. Int J Epidemiol 1981;**10**(4):337-41